Clinical Laboratory Improvement Advisory Committee
Subcommittee on Test Categorization Meeting

January 29, 1993

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The Clinical Laboratory Improvement Advisory Committee's (CLIAC) Subcommittee on Test Categorization met at the Centers for Disease Control and Prevention (CDC) Auditorium A in Atlanta, Georgia, on January 29, 1993. Those in attendance are listed below:

MEMBERS PRESENT

Ms. Michele Best
Dr. Stanley Inhorn
Dr. Stephen Kroger
Dr. Morton Schwartz

Ex Officio Members

Dr. Carlyn Collins, CDC
Dr. Steven Gutman, FDA
Ms. Judith Yost, HCFA

Executive Secretary

Dr. Edward Baker

Centers for Disease Control

Ms. Rosemary Bakes-Martin
Mr. James Bloom
Dr. Joe Boone
Mr. Henry Colvin
Ms. Carol Cook
Ms. Iris Dixon
Mr. Tom Hearn
Mr. Edwin Holmes
Dr. Devery Howerton
Mr. Kevin Malone
Ms. Marta Ramirez
Dr. John Ridderhof
Ms. Rhonda Whalen

Contract Consultants

Dr. Frederick Meier
Dr. John Ross
Dr. Don Wiebe

Invited Presentations

Dr. Fred Lasky
Dr. George Nankervis

Oral Presentations

Ms. Erika Ammirati
Mr. Randy Fenniger
Ms. Jean Zych

Estimated Number of Public in Attendance: 50

INTRODUCTION TO THE CLIAC SUBCOMMITTEE MEETING

The CLIAC Subcommittee members were welcomed by Edward L. Baker, M.D., Director, Public Health Practice Program Office (PHPPO), CDC, Executive Secretary of the Subcommittee.
Additional welcoming remarks were made by the Chairman of the Subcommittee, J. Stephen Kroger, M.D., Chief Executive Officer, Commission on Office Laboratory Accreditation.

The Chairman of the Subcommittee gave the charge to the Subcommittee and addressed Subcommittee responsibilities and protocol.

- The Subcommittee, formed at the direction of CLIAC to consider specific issues relative to test categorization, will make recommendations to the full committee (CLIAC) in regard to criteria for classifying waived tests, physician-performed microscopy procedures, and moderate and high complexity tests; application of criteria to specific tests; and the impact of the test categorization process on access to laboratory testing, and patient diagnosis and therapy.

- Recommendations of the Subcommittee are not to be considered as final recommendations until approved by the full committee. In issues with no consensus, the Chairman will present the pros and cons to the CLIAC. The chairman of the Subcommittee will present a report of this meeting at the next meeting of the full committee (February 17-18, 1993).

- Contract consultants will be participants in the Subcommittee meetings as needed to supplement expertise in the areas under discussion.

- Health and Human Services, employees of the CDC, the Food and Drug Administration (FDA), and the Health Care Financing Administration (HCFA) will participate, as necessary, to provide status information on issues under consideration. These participants are not voting members.

- At the request of the Chairman, an additional member from the full committee, with particular expertise in the area of discussion, may be asked to particular in the Subcommittee meeting.

- Due to the small size of the Subcommittee, the Chairman will turn the chair over to the Executive Secretary of the Subcommittee prior to participating in the discussion of the issue under consideration.

- Issues will be presented that will require members to:

  - listen and participate in discussion;

  - ask questions and identify options;

  - consider impact of any option on quality and availability of testing; and

  - provide rationale for any recommendations.

- A call to vote may be made by the Chairman or the Subcommittee members.
- Issues for this first Subcommittee meeting were selected because of substantive comment received and the need for additional information and analysis.

- Public comments relating to test categorization will be heard after completion of the scheduled topics. The number and length of the public comments will be determined by the time available.

THE ISSUES AND TEST CATEGORIZATION PROCESS

Carlyn L. Collins, M.D., Director, Division of Laboratory Systems (DLS), PHPPO, CDC, gave an overview of the test categorization process, including an explanation of the criteria employed and methodology for scoring (See Addendum A). In addition to the overview, Dr. Collins noted that a compilation of all categorized test systems will be published in the Federal Register in the near future. This presentation provided background information and preceded the presentations and discussions of the issues included on the agenda for this meeting. These issues included:

- A review of the categorization of high density lipoprotein (HDL) cholesterol test systems;

- Consideration of the Gram stain and Tzanck test for inclusion in the physician-performed microscopy category; and

- A review of direct antigen tests for Group A Streptococcus.

For each issue, CDC provided a technical overview which outlined the application of test categorization criteria in scoring test systems in determining the test category. In addition, test utility and clinical impact were addressed by a CDC contract consultant, as necessary.

The Executive Secretary of the Subcommittee clarified that for the purposes of the Subcommittee's deliberations, the criteria for test categorization would be accepted as published in the Federal Register.

HDL CHOLESTEROL TEST SYSTEM CATEGORIZATION

I. PRESENTATIONS

The technical presentation was made by D. Joe Boone, Ph.D., Assistant Director for Science, DLS, PHPPO, CDC. The clinical/impact presentations were made by Donald A. Weibe, Ph.D., Associate Professor, Pathology and Laboratory Medicine, University of Wisconsin, Madison, WI; John W. Ross, M.D., Director, Department of Pathology and Clinical Laboratories, Kennestone Hospital, Marietta, GA; and Fred D. Lasky, Ph.D., Director, Government and Industry Relations, Clinical Products Division, Eastman Kodak Company, Rochester, NY (See Addendum B).

II. ISSUE

- Should some high complexity HDL cholesterol procedures be recategorized as moderate complexity?

III. DISCUSSION

Follow-up Questions to Presentations

The Chairman noted that at the first CLIAC meeting, members expressed reservations about focusing on specific test systems, but for the purpose of the Subcommittee's deliberations concerning categorization of HDL cholesterol test systems, the Kodak Ektachem DT 60 will serve as the index case for review.

Early discussion consisted of Subcommittee members making comments and asking specific questions of CDC and the contract consultants regarding proficiency testing (PT) performance, personnel qualifications, and technical issues concerning sample pretreatment. With respect to PT performance, it was noted that PT data reflected no significant differences between desktop analyzers and larger instruments. PT data is not currently evaluated in a manner that will distinguish differences in PT performance between those test systems in which the pretreatment step is operator-dependent and those in which pretreatment is performed by the test system and is not operator-dependent. Although the coefficient of variation (CV) of HDL cholesterol PT results varies greatly between laboratories as well as among test methodologies, it was pointed out that the PT samples are variable which may attribute to the wide disparity in CV results. There was some dialogue about categorizing tests as high complexity with the potential for the qualification requirements for high complexity testing personnel and laboratory director creating a barrier that would limit access to HDL cholesterol testing.

In addition, Subcommittee members asked specific questions concerning the Kodak Ektachem DT 60. Does the instrument reject turbid samples, use serum and/or plasma samples, and what differences exist between the DT 60 and the Ektachem 700? In response, it was stated that the DT 60 does not reject turbid samples, presently uses serum samples exclusively rather than plasma or serum and few differences in methodologies exist between the Ektachem 700 and the DT 60.

The Chairman asked whether any attendees wished to make a brief statement concerning HDL cholesterol test system categorization. Paul M. Fischer, M.D., Professor, Department of Family Medicine, Medical College of Georgia, representing the American Academy of Family Practice and Carolyn George, Regulatory Affairs, DuPont provided comments (See Addendum C).

Review and Discussion of the Test Categorization Criteria Scores for the Kodak Ektachem DT 60

The Executive Secretary initiated the test categorization discussion of the index case, Kodak Ektachem DT 60, by focusing the Subcommittee's attention on two issues: 1) Did CDC correctly apply the test categorization process; and 2) Are there factors (e.g., access to testing) in addition to the seven criteria which should be considered in test categorization?

The Subcommittee concentrated on reviewing the three criteria related to cognitive skills; knowledge, training/experience, and interpretation/judgment. There was limited discussion of the other four criteria; reagent/material preparation, step complexity, availability of calibration/quality control (QC)/PT materials, and troubleshooting/maintenance.

The Subcommittee articulated the need to distinguish the differences between the basic knowledge required as a prerequisite for testing and the specific knowledge and skills acquired during training or over time with experience. There was extensive discussion on the amount and type of training required for performing the operational steps and the judgment and interpretation required for decision-making during the performance of HDL cholesterol testing. Subsequent to these discussions, the Subcommittee was split on lowering the score for knowledge from a 2 to 1. Three Subcommittee members were in agreement that the scores for training/experience and interpretation/judgment should be lowered from a 3 to a 2. No changes were recommended for the other four criteria.

The Subcommittee considered the potential impact on laboratories, if some analytes performed on multichannel instruments were categorized as moderate complexity while others were categorized as high complexity. Also, the limitations of using PT data, at this time, to evaluate the accuracy of HDL cholesterol test methodologies were discussed. A Subcommittee member observed that, due to the large number of physician office laboratories (POLS) (i.e., currently 80,000 POLs out of a total of 120,000 laboratories are registered under the Clinical Laboratory Improvement Amendments of 1988), any decisions concerning a regulatory framework for laboratories will, of necessity, need to address the unique characteristics of POL testing. In addition, the POL testing environment has benefited from technological advances in test systems and initial efforts in complying with Federal requirements for training and employment of qualified personnel, enrollment and participation in PT programs and performance of QC practices.

IV. RECOMMENDATIONS

The Subcommittee will recommend to CLIAC that, based on its review, the Kodak Ektachem DT 60 HDL cholesterol test system be recategorized from high to moderate complexity. In addition, this evaluation may serve as a basis for review of similarly scored HDL cholesterol test systems.

PHYSICIAN-PERFORMED MICROSCOPY PROCEDURES

I. PRESENTATION

Carlyn L. Collins, M.D., of CDC, provided an update on the status of the physician-performed microscopy category which was created based on recommendations from the first CLIAC meeting. She noted that this category of tests was added to the regulations on January 19, 1993 by publication in the Federal Register, which, at §493.16, listed the tests currently included in this category and the criteria used for categorization. In addition, she discussed applying the aforementioned criteria to the two procedures referred to this Subcommittee by CLIAC for possible inclusion in the physician-performed microscopy category (See Addendum D).

II. ISSUE

- Should the Gram stain and Tzanck test be included in the physician-performed microscopy category?

III. DISCUSSION

Gram Stain

It was generally agreed that the discussion be limited only to those smears (i.e., cervical/urethral smears) categorized as moderate complexity. A Subcommittee member noted that physicians are trained to perform Gram stains and rely on Gram stain results for immediate diagnosis and treatment of patients. The other Subcommittee members agreed that physicians, access to testing is a consideration and this category was created to address those procedures performed by physicians as part of the medical examination; however, for inclusion in this category, all criteria must be met. In addition, concern was expressed that not all physicians receive sufficient training to properly perform and interpret Gram stains. Three Subcommittee members agreed that cervical/urethral Gram stains do not meet the criteria for inclusion in the physician-performed microscopy category. One Subcommittee member felt that cervical/urethral Gram stains should be included in the physician-performed microscopy category.

Tzanck Test

All Subcommittee members agreed that the Tzanck test requires a higher level of knowledge and training than that required for the Gram stain. In addition, the Tzanck test is not a routine procedure and physicians may not receive training for the performance and interpretation of the test. The Subcommittee noted that certain medical specialists (e.g. dermatologists) use this procedure routinely and are trained to perform the Tzanck test as part of their medical residency. As a reminder, a Subcommittee member noted that the full committee recommended that the physician-performed microscopy category not include any tests that are limited to performance by a particular medical specialty. in response, one Subcommittee member agreed that CLIAC had made that initial determination, but felt that the criteria for physicianperformed microscopy categorization was a barrier to the inclusion of those tests specifically performed by certain medical specialties; and this issue should be reconsidered by CLIAC. All Subcommittee members agreed that the Tzanck test does not meet all the criteria for inclusion in the physician-performed microscopy category.

IV. RECOMMENDATIONS

The Subcommittee will recommend to CLIAC, based on its review, not to include the Gram stain and Tzanck test on the list of physician-performed microscopy procedures.

DIRECT ANTIGEN GROUP A STREPTOCOCCUS TESTS

I. PRESENTATIONS

The technical presentation was made by John C. Ridderhof, Dr. P.H., Chief, Laboratory Practice Standards Branch, DLS, PHPPO, CDC. The clinical/impact presentations were made by Frederick A. Meier, M.D., Department of Pathology, A.I. DuPont Institute, Children's Hospital, Wilmington, DE; and George A. Nankervis, Ph.D., M.D., Chairman of Pediatrics, Children's Hospital Medical Center of Akron, Akron, OH (See Addendum E).

II. ISSUE

- Should rapid strep tests be included in the physicianperformed microscopy category?

III. DISCUSSION

Preliminary discussion was limited to Subcommittee asking presenters to clarify data included in their presentations.

The Chairman asked whether any attendees wished to make a brief statement concerning direct antigen tests for Group A Streptococcus. Paul M. Fischer, M.D., Professor of Medicine, Medical College of Georgia, representing the American Academy of Family Practice provided comments (See Addenda C and F).

Subcommittee members all agreed that rapid strep tests do not meet the criteria for inclusion in the physician-performed microscopy category. The Executive Secretary pointed out that, inasmuch as the physician-performed microscopy category has just been added to the regulations, it may be prudent to await public comment on the criteria and the tests included in the category.

One of the presenters requested the Subcommittee to consider adding rapid strep tests to the waived category. The Executive Secretary reviewed the second criterion for waived tests, ,test systems are simple laboratory examinations and procedures which employ methodologies that are so simple and accurate as to render the likelihood of erroneous results negligible," for the Subcommittee's consideration in determining whether to include these procedures in the waived category.

Three Subcommittee members felt that the risk associated with false positive and false negative rapid strep test results was not negligible, and quality control is necessary for these procedures and would not be required if rapid strep tests were placed in the waived category. It was noted that there are currently thirty-five different test systems for performing rapid strep tests that employ a variety of methodologies [e.g., latex agglutination, enzyme-linked immunosorbent assay (ELISA)] and vary in terms of accuracy and simplicity. The Subcommittee was concerned about its ability to evaluate <u>all</u> rapid strep tests for possible waiver due to the heterogeneity of test system methodologies and subsequent variability in the sensitivity and specificity of the test systems.

The first criterion for waived tests: "cleared by FDA for home uses was discussed as a mechanism for achieving waived status. It was pointed out that manufacturers may desire waived status for a test system used in laboratories and would not seek FDA clearance for home use. The Executive Secretary explained that CDC reviewed test systems cleared by the FDA for home use to ensure that, they met the other criteria prior to

assigning them to the waived test list. Two Subcommittee members suggested that the waived test criteria need to be more definitive, with one of the Subcommittee members favoring another approach for categorizing waived tests.

The Executive Secretary summarized the discussion by stating that three Subcommittee members were in agreement that rapid strep tests should not be added to the waived category, while one Subcommittee member suggested that a subset of these tests might have a different performance history and therefore could be considered after the waived test criteria were more definitive.

IV. RECOMMENDATIONS

- The Subcommittee will recommend to CLIAC, based on its review, not to include rapid strep tests on the list of physician-performed microscopy procedures.

- Based on the current criteria, the Subcommittee could not support the addition of rapid strep tests to the waived category.

PUBLIC COMMENTS

In response to the Federal Register notice published January 13, 1993, announcing the CLIAC Subcommittee on Test Categorization meeting, the following individuals requested permission and were granted the opportunity to make an oral presentation. Time was allotted at the conclusion of each presentation for the Subcommittee to ask for clarification or make observations concerning the presentation. (See Addendum F for the written materials prepared and submitted to the Subcommittee by individuals making a presentation.)

Erika B. Ammirati
Manager, Clinical and Regulatory Affairs
Technical Communications
CHEMTRAK
Sunnyvale, CA

Jean Zych
Vice President of Marketing
Wampole Laboratories
Cranbury, NJ

Randy Fenniger, J.D.
Senior Vice President
MARC Associates
Washington, D.C.
Representing the American Urological Association

GENERAL COMMENTS

- Morton K. Schwartz, Ph.D., chairman of the CLIAC, was a substitute for Subcommittee member, Paul Bachner, M.D., who was unable to attend the January 29, 1993 meeting.

- Future issues may be referred to this Subcommittee by CLIAC, as a result of discussions held at a meeting of the full committee; the CLIAC chairman; or the CLIAC Executive Secretary.

I certify that this summary report of the January 29, 1993, meeting of the Clinical Laboratory Improvement Advisory Committee's Subcommittee on Test Categorization is an accurate and correct representation of the meeting.

J. Stephen Kroger, M.D.
Chair